X

Docket No. 46342/55862 Page 4 of 7

fragment, cDNA was synthesized from 1 µg of mouse brain poly(A)⁺ RNA in a manner similar to Example 5, using Marathon cDNA Amplification Kit (Clontech) to use the cDNA as a template. The following three primers were synthesized and used in combination with AP1 primer attached to the kit for PCR.--

Please replace the paragraph at page 183, lines 23-25, with the following paragraph:



--(1) Cloning of the cDNA encoding the rat "area around brainstem"-derived G protein-coupled receptor protein and determination of the base sequence--

REMARKS

Applicants request the Examiner to enter the changes in the specification requested above. These changes are due to inadvertent translation errors, which are hereby corrected.

In view of the foregoing amendments and remarks, the present application is respectfully considered in condition for allowance. An early reconsideration and notice of allowance are earnestly solicited.

Although it is not believed that any additional fee is required to consider this submission, the Commissioner is hereby authorized to charge our deposit account no. 04-1105 should any fee be deemed necessary.

Respectfully submitted,

Date: January 7, 2002

Kathryn A. Piffat, Ph.D. (Reg. No. 34,901) Dike, Bronstein, Roberts & Cushman

Intellectual Property Practice Group of

EDWARDS & ANGELL, LLP

P.O. Box 9169 Boston, MA 02209 (617) 439-4444

BOS2_186010.1

Docket No. 46342/55862 Page 5 of 7

<u>APPENDIX I</u>

REVISIONS OF THE SPECIFICATION PURSUANT TO REVISED RULE § 1.121 In the specification:

The paragraph at page 95, lines 10-12, should be replaced with the following paragraph:

(6) oversecretion of amylase accompanied by endoscopic cholangio pancreatography [and for the postoperative treatment in pancreas surgery];

The paragraph at page 95, line 28, to page 96, line 6, should be replaced with the following paragraph:

(9) tumor or cancer (e.g., thyroid cancer, colon cancer, breast cancer, prostatic cancer, small cell lung cancer, non-small cell lung cancer, pancreatic cancer, gastric cancer, bile duct cancer, liver cancer, bladder cancer, ovary cancer, melanoma, osteosarcoma, chondrosarcoma, malignant pheochromocytoma, neuroblastoma, brain tumor, thymoma, kidney cancer, etc.), leukemia (e.g., leukemia/chronic lymphoid leukemia of basophil leukocyte, chronic myeloid leukemia, Hodgkin's disease, non-Hodgkin's lymphoma, etc.)[, these agents may also be used alone or in combination with other carcinostatic agents (e.g., tamoxifen, LHRH agonist, LHRH antagonist, interferon-α, β, and γ, interleukin-2, etc.)];

The paragraph at page 149, line 29, to page 150, line 15, should be replaced with the following paragraph:

More specifically, the desired gene can be obtained by retrieval of database using as a probe the RFG(R/K) sequence or RSG(R/K) sequence or RLG(K/R) sequence or a sequence containing the amino acid sequence and a sequence containing the base sequence encoding the same. Examples of the probe include:

 $RFGK: \ 5'-(C/A)G(A/C/G/T)TT(T/C)GG(A/C/G/T)AA(A/G)-3' \ (SEQ \ ID \ NO:20)$

RFGR: 5'-(C/A)G(A/C/G/T)TT(T/C)GG(A/C/G/T)(A/C)G(A/C/G/T)-3' (SEQ ID

NO:21)

R[s]SGK: 5'-(C/A)G(A/C/G/T)(A/T)(C/G)(A/C/G/T)GG(A/C/G/T)AA(A/G)-3' (SEQ ID NO:22)

Docket No. 46342/55862 Page 6 of 7

RSGR: 5'-

(C/A)G(A/C/G/T)(A/T)(C/G)(A/C/G/T)[(A/C)G(A/C/G/T)AA(A/G)]GG(A/C/G/T)(A/C)G(A/C/G/T)-3' (SEQ ID NO:23)

RLGK: 5'-(C/A)G(A/C/G/T)(T/C)T(A/C/G/T)[AA(A/G)]GG(A/C/G/T)AA(A/G)-3' (SEQ ID NO:24)

RLGR: 5'-(C/A)G(A/C/G/T)(T/C)T(A/C/G/T)GG(A/C/G/T)(A/C)G(A/C/G/T)-3' (SEQ ID NO:25)

and the like, as the DNA sequence corresponding to RFG(K/R), RSG(K/R) and RLG(K/R).

The paragraph at page 166, lines 28-32, should be replaced with the following paragraph:

This shows the base sequence of primer 1 used for cloning the cDNA encoding the rat [cerebellum] "area around brainstem"-derived novel G protein-coupled receptor protein rOT7T022L obtained in Example 7, which will be later described. [SEQ ID NO:36]

The paragraph at page 174, line 23, to page 175, line 12, should be replaced with the following paragraph:

The reaction solution was composed of 20 pM each of the synthetic DNA primers (F5 and hR1), 0.25 mM dNTPs, 0.5 ml of Ex Taq DNA polymerase and a buffer attached to the enzyme, which were mixed together to make the total volume of the reaction solution 50 ml. Using Thermal Cycler (Perkin-Elmer Co.) for amplification, one cycle was set to include 98°C for 10 seconds, 65°C for 20 seconds and 72°C for 20 seconds. This cycle was repeated 40 times in total. The amplification product was confirmed by 1.2% agarose electrophoresis and ethidium bromide staining. After the PCR product was proven to be amplified, the reaction product was purified using [QUIA] QIA Quick PCR Purification Kit [(Quiagen)] (Qiagen), followed by sequencing. The sequencing reaction was conducted using BigDye Deoxy Terminator Cycle Sequence Kit (ABI Inc.). The DNAs were decoded using an automated fluorescent sequencer (ABI377). The data of the base sequences obtained were read by DNASIS (Hitachi System Engineering Co., Ltd.). As a result, cDNA with the 3' terminus different from the cDNA obtained in

Docket No. 46342/55862 Page 7 of 7

Example 2 was obtained. The cDNA thus obtained in this Example was found to be a splicing variant of the cDNA obtained in Example 2. The base sequence determined (SEQ ID NO:9) and the deduced amino acid sequence (SEQ ID NO:8) are shown in FIG. 3.

The paragraph at page 181, lines 11-25, should be replaced with the following paragraph:

Further using the same primer set, PCR was carried out by repeating [39] <u>25</u> times a cycle set to include 98°C for 10 seconds, 60°C for 20 seconds and 72°C for 25 seconds. The amplification product was confirmed by 1.2% agarose gel electrophoresis and ethidium bromide staining. The band was purified using QIA quick Gel Extrication Kit [(Quiagen)] (Qiagen), followed by sequencing in a manner similar to Example 3. To obtain the 5' and 3' terminal sequences of the mouse type physiologically active peptide cDNA fragment, cDNA was synthesized from 1 µg of mouse brain poly(A)⁺ RNA in a manner similar to Example 5, using Marathon cDNA Amplification Kit (Clontech) to use the cDNA as a template. The following three primers were synthesized and used in combination with AP1 primer attached to the kit for PCR.

The paragraph at page 183, lines 23-25, should be replaced with the following paragraph:

(1) Cloning of the cDNA encoding the rat [cerebellum] "area around brainstem"-derived G protein-coupled receptor protein and determination of the base sequence

BOS2_186010.1